12/29/99

AUTHOR ADDRESS: (a)Dep. Med., Johns Hopkins Univ. Sch. Med., Ross Build. 618, 720 Rutland Ave., Baltimore, MD 21205**USA
JOURNAL: Developmental Brain Research 90 (1-2):p45-53 1995
ISSN: 0165-3806
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09859754 BIOSIS NO.: 199598314672
Hematologic Consequences of Borna Disease Virus Infection of Rat Bone Marrow and Thymus Stromal Cells.
AUTHOR: **Rubin Steven A**; Sierra-Honigmann Ana M; Lederman Howard M; Waltrip Royce W Ii; Eiden Joseph J; Carbone Kathryn M(a
AUTHOR ADDRESS: (a)Johns Hopkins Univ. Sch. Med., Ross 1159, 720 Rutland Ave., Baltimore, MD 21205**USA
JOURNAL: Blood 85 (10):p2762-2769 1995
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08820566 BIOSIS NO.: 199395109917
Characterization of a glial cell line persistently infected with Borna disease virus (BDV): Influence of neurotrophic factors on BDV protein and RNA expression.
AUTHOR: Carbone Kathryn M(a); **Rubin Steven A**; Sierra-Honigmann Ana A; Lederman Howard M
AUTHOR ADDRESS: (a)Div. Infectious Diseases, Dep. Med., Johns Hopkins Univ. Sch. Med., Baltimore, MD 21287**USA
JOURNAL: Journal of Virology 67 (3):p1453-1460 1993
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

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? s (vla(w)4 or alpha4) and (encephalitis)(20n)(herpes or arbovirus)
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          4211  VLA(W)4
          3879  ALPHA4
         54792  ENCEPHALITIS
        128481  HERPES
         20373  ARBOVIRUS
          8207  ENCEPHALITIS(20N)(HERPES OR ARBOVIRUS)
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               ARBOVIRUS)
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          3879  ALPHA4
        128481  HERPES
         20373  ARBOVIRUS
      S7    95  (VLA(W)4 OR ALPHA4) AND(HERPES OR ARBOVIRUS)
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      S9       0  S8 AND ENCEPHALITIS
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 8/3/1      (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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t s8/7/1-12

8/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13255431 BIOSIS NO.: 200100462580
Herpes simplex virus US3 and ICP4 as inhibitors of apoptosis.
AUTHOR: Leopardi Rosario(a); Roizman Bernard
AUTHOR ADDRESS: (a)Chicago, IL**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1245 (3):pNo Pagination Apr. 17, 2001
MEDIUM: e-file
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The ICP4 protein of **herpes** simplex virus plays an important role in the transactivation of viral genes. The present invention discloses that ICP4 also has the ability to inhibit apoptosis. This function appears to reside in functional domain distinct from the transactivating function, as indicated by studies using temperature sensitive mutants of ICP4 that transactivating function at elevated temperatures. Also disclosed are methods for inhibition of apoptosis using ICP4 or an ICP4 encoding gene, such as an **alpha4** gene, methods of inhibiting ICP4's apoptosis-inhibiting function, and methods for the production of recombinant proteins and treatment of HSV infections. Further, the present invention discloses that the HSV-1 mutant lacking the **alpha4** gene, has a secondary mutation in the gene Us 3 specifying a protein kinase. Thus a functional Us 3, a viral gene encoding a protein kinase known to phosphorylate serine/theonine within a specific arginine rich consensus sequence, is required in order to block apoptosis. Also disclosed are methods for inhibition of apoptosis using Us 3 or an Us 3 encoding gene, methods of inhibiting Us 3's apoptosis-inhibiting function and methods for the production of recombinant proteins and treatment of HSV infections.

8/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13254960 BIOSIS NO.: 200100462109
The Us3 protein kinase of **herpes** simplex virus 1 mediates the posttranslational modification of BAD and prevents BAD-induced programmed cell death in the absence of other viral proteins.
AUTHOR: Munger Joshua; Roizman Bernard(a)
AUTHOR ADDRESS: (a)Marjorie B. Kovler Viral Oncology Laboratories, University of Chicago, 910 East 58th Street, Chicago, IL, 60637: bernard@cummings.uchicago.edu**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 98 (18):p10410-10415 August 28, 2001
MEDIUM: print
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Earlier studies have shown that the d120 mutant of **herpes** simplex virus 1, which lacks both copies of the **alpha4** gene, induces apoptosis in all cell lines tested. In some cell lines d120-induced apoptosis, manifested by the release of cytochrome c,

activation of caspase 3, and fragmentation of cellular DNA, is blocked by the overexpression of Bcl-2. In these cells viral protein kinase Us3 delivered in trans blocks apoptosis induced by the mutant virus at a premitochondrial stage. We report that the Us3 protein kinase targets the pro-apoptotic BAD member of the Bcl-2 family. Specifically, the Us3 protein kinase mediates a posttranslational modification of BAD and blocks its cleavage, which is reported to activate apoptosis. Thus, Us3 protein kinase is the sole viral protein required to block activation of caspase 3, prevent cleavage of poly(ADP-ribose) polymerase, and block fragmentation of cellular DNA induced by BAD.

8/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13119578 BIOSIS NO.: 200100326727
The US3 protein kinase blocks apoptosis induced by the d120 mutant of **herpes** simplex virus 1 at a premitochondrial stage.
AUTHOR: Munger Joshua; Chee Ana V; Roizman Bernard(a)
AUTHOR ADDRESS: (a)The Marjorie B. Kovler Viral Oncology Laboratories, The University of Chicago, 910 E. 58th St., Chicago, IL, 60637: bernard@cummings.uchicago.edu**USA
JOURNAL: Journal of Virology 75 (12):p5491-5497 June, 2001
MEDIUM: print
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Earlier studies have shown that the d120 mutant of **herpes** simplex virus 1, which lacks both copies of the **alpha4** gene, induces caspase-3-dependent apoptosis in HEp-2 cells. Apoptosis was also induced by the **alpha4** rescuant but was blocked by the complementation of rescuant with a DNA fragment encoding the Us3 protein kinase (R. Leopardi and B. Roizman, Proc. Natl. Acad. Sci. USA 93:9583-9587, 1996, and R. Leopardi, C. Van Sant, and B. Roizman, Proc. Natl. Acad. Sci. USA 94:7891-7896, 1997). To investigate its role in the apoptotic cascade, the Us3 open reading frame was cloned into a baculovirus (Bac-Us3) under the control of the human cytomegalovirus immediate-early promoter. We report the following. (i) Bac-Us3 blocks processing of procaspase-3 to active caspase. Procaspase-3 levels remained unaltered if superinfected with Bac-Us3 at 3 h after d120 mutant infection, but significant amounts of procaspase-3 remained in cells superinfected with Bac-Us3 at 9 h postinfection with d120 mutant. (ii) The Us3 protein kinase blocks the proapoptotic cascade upstream of mitochondrial involvement inasmuch as Bac-Us3 blocks release of cytochrome c in cells infected with the d120 mutant. (iii) Concurrent infection of HEp-2 cells with Bac-US3 and the d120 mutant did not alter the pattern of accumulation or processing of ICP0, -22, or -27, and therefore Us3 does not appear to block apoptosis by targeting these proteins.

8/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12950580 BIOSIS NO.: 200100157729
An HSV-vector expressing glutathione peroxidase protects against kainic acid-mediated neuronal death.
AUTHOR: McIntosh L J(a); Patel R J; Nimon T Y; McLaughlin J R; Sapolsky R M
AUTHOR ADDRESS: (a)Stanford University, Stanford, CA**USA

JOURNAL: Society for Neuroscience Abstracts 26 (1-2):pAbstract No-7728
2000
MEDIUM: print
CONFERENCE/MEETING: 30th Annual Meeting of the Society of Neuroscience New
Orleans, LA, USA November 04-09, 2000
SPONSOR: Society for Neuroscience
ISSN: 0190-5295
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Glutathione Peroxidase (GSPx) is an important antioxidant enzyme in neurons, converting potentially damaging peroxides into water and playing a role in protecting membranes against oxygen radical damage. This study examines the possible protective effect of overexpressing GSPx against excitotoxic insult in rat mixed hippocampal primary cultures. We created a **Herpes** Simplex Virus Amplicon expressing GSPx under the **herpes alpha4** promoter. Cultures were infected for 16 hours infection with the HSV-GSPx vector before assaying for GSPx activity with a spectrophotometer. Over different vector concentrations, GSPx was increased from 10 to 20% in these cells. Kainic Acid (KA), an excitotoxic insult, causes increased oxygen radical production. Cultures were infected with HSV-GSPx and then exposed to both 50muM and 100muM concentrations of KA. Then, after 24 hours, the tissue was fixed and assayed for neuronal survival by antibody staining for MAP2, a protein found only in intact neurons. A colormetric staining technique allowed for the measurement of whole well neuronal survival. Neuroprotection was analyzed by comparing against a control vector expressing beta-galactosidase only. GSPx increased neuronal survival by 15-30% over the control vector. These results suggest that GSPx may be useful to protect against excitotoxic damage. Further studies are planned to correlate overexpression of GSPx and oxygen radical production after an insult. Supported by NIH grant ROI NS32848 and Howard Hughes Undergraduate Research Grant.

12868597 BIOSIS NO.: 200100075746
Model for examining neuroprotection in human brain tissue.
AUTHOR: Bottino C J(a); Howard S A; Steinberg G; Sapolsky R M
AUTHOR ADDRESS: (a)Stanford University, Stanford, CA**USA
JOURNAL: Society for Neuroscience Abstracts 26 (1-2):pAbstract No-9418
2000
MEDIUM: print
CONFERENCE/MEETING: 30th Annual Meeting of the Society of Neuroscience New
Orleans, LA, USA November 04-09, 2000
SPONSOR: Society for Neuroscience
ISSN: 0190-5295
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: This preliminary study examines the use of viral vectors to over-express potentially neuroprotective genes in human brain tissue. Previous experiments indicate the effectiveness with which this approach decreases damage in rat neurons, both in vitro and in vivo. Success in the rodent model led to an investigation of an analogous approach with human neural tissue. An effective model must include: tissue viability, a measure of damage caused by insult, and expression of the neuroprotective gene. We used a replication deficient **Herpes** Simplex amplicon (HSV), lacking the **alpha4** gene and used in prior rat studies, as

the vector to deliver the plasmid into tissue. The brain samples were generally healthy, and were excised during surgical procedures from cortical regions overlying diseased tissue. Approximately 20 minutes after surgery, the samples were micro-pump injected with the vector, sliced to 300 mum, and incubated for approximately 24 hours in artificial cerebral-spinal fluid. Metabolic measurements were taken at various time points. We have demonstrated stable metabolism over at least 24 hours according to microphysiometric measurements. ATP assays showed substantial metabolic decline following glutamate exposure. 24 hours following microinjection of the HSV carrying a beta-gal plasmid, we saw significant beta-gal expression. Through these experiments, we have established a foundation with which to test a viral vector method for protection in the human model. Funding was supplied by the Adler Foundation

8/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12842471 BIOSIS NO.: 200100049620
Synthesis, subcellular localization and VP16 interaction of the **herpes** simplex virus type 2 UL46 gene product.
AUTHOR: Kato K; Daikoku T; Goshima F; Kume H; Yamaki K; Nishiyama Y(a)
AUTHOR ADDRESS: (a)Research Institute for Disease Mechanism and Control, Nagoya University School of Medicine, Nagoya, 466-8550**Japan
JOURNAL: Archives of Virology 145 (10):p2149-2162 2000
MEDIUM: print
ISSN: 0304-8608
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: We developed a rabbit polyclonal antiserum reactive against a recombinant 6x His-UL46 fusion protein expressed in Escherichia coli, and using this antiserum identified the UL46 gene product of **herpes** simplex virus type 2 (HSV-2) to be phosphoproteins with apparent molecular masses of 82-, 84-, and 86-kDa in infected Vero cells. The UL46 protein was produced in the late phase of infection in a manner highly dependent on viral DNA synthesis, and was mainly distributed at the edge of the nucleus in the cytoplasm. Although its kinetics of production and its progress of distribution were different from those of the major tegument protein VP16 (the UL48 gene product or alpha-trans-inducing factor (alphaTIF)), most of the UL46 protein colocalized with VP16 in the late phase of infection, and copurified with it in column chromatography. Moreover, our data showed that the HSV-2 UL46 protein, when coexpressed with VP16, enhanced **alpha4** promotor-regulated gene expression in a transient luciferase reporter assay, while the expression of the UL46 protein alone suppressed it.

8/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12124196 BIOSIS NO.: 199900419045
Heat stress activates production of **herpes** simplex virus type 1 from quiescently infected neurally differentiated PC12 cells.
AUTHOR: Danaher Robert J; Jacob Robert J; Chorak Mario D; Freeman Chris S; Miller Craig S(a)
AUTHOR ADDRESS: (a)Department of Oral Health Practice, University of Kentucky College of Dentistry, 800 Rose Street, Oral Medicine Section MN 118, Lexington, KY, 40536-0297**USA

JOURNAL: Journal of Neurovirology 5 (4):p374-383 Aug., 1999
ISSN: 1355-0284
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: We have previously described a novel in vitro model of a non-productive **herpes** simplex virus type 1 (HSV-1) infection in neurally differentiated (Nd)-PC12 cells that allows for inducible virus replication upon forskolin treatment. In this study, we further characterized the quiescent state of infection and examined the ability of heat stress (HS) to induce virus from this non-productive state. These studies demonstrated that (i) the quiescent state is characterized by the absence of cell-associated virus, capsids, and viral antigens; (ii) HS (43degreeC, 3 h) efficiently activated virus from quiescently infected Nd-PC12 (QIF-PC12) cells; (iii) the rate of virus production was significantly greater following HS than forskolin treatment, and the rates of both were dependent on MOI; (iv) forskolin and HS appeared to affect pathways of viral activation from a quiescent state as they did not enhance viral growth in Nd-PC12 cells; (v) viral **alpha4** gene and host HSP72 gene transcription were rapidly induced in QIF-PC12 as soon as 3 h post-HS initiation; (vi) induction of the viral alpha27 gene followed that of representative beta and gamma genes, UL30 and UL18, respectively, and (vii) HS induced asynchronous HSV-1 replication from QIF-PC12 cells with 1:400 to 1:22 000 positive foci detected as rapid as 24 h post-induction when established at MOIs of 30 and 3, respectively. These findings provide evidence that **alpha4** may be involved in the switch from quiescence to productive infection. Furthermore, this model has the potential to advance our understanding of how HS initiates the HSV-1 productive cycle from a cryptic viral genome.

8/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12093338 BIOSIS NO.: 199900388187
Establishment of a quiescent **herpes** simplex virus type 1 infection in neurally-differentiated PC12 cells.
AUTHOR: Danaher Robert J; Jacob Robert J; Miller Craig S(a)
AUTHOR ADDRESS: (a)Oral Medicine Section MN 118, Department of Oral Health Practice, University of Kentucky College**USA
JOURNAL: Journal of Neurovirology 5 (3):p258-267 June, 1999
ISSN: 1355-0284
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Rat pheochromocytoma (PC12) cells differentiated with nerve growth factor (Nd-PC12) were used to investigate the establishment of a non-productive **herpes** simplex virus type 1 (HSV-1) infection that is reversible. The results of this work are as follows: (i) Nd-PC12 cultures could be maintained as long term (>7 weeks) non-dividing cultures only when plated on collagen-coated dishes in the absence of serum; (ii) Infection of Nd-PC12 with HSV-1 strains KOS and 17 in the transient presence of acycloguanosine (ACV) resulted in all cultures free of detectable levels of infectious virus at the time of ACV removal and ACV was not needed to maintain the non-productive quiescent state in the subsequent 8 weeks; (iii) These persistently infected and quiescent (QIF)-PC12 cultures demonstrated both spontaneous and forskolin-inducible virus production, at low (5%) and high frequencies (92-100%), respectively during the first 2 weeks post-ACV withdrawal. (iv) In

contrast to other in vitro models, HSV-1 failed to reactivate following removal of nerve growth factor. (v) A high percentage of QIF-PC12 cultures (50-100%) produced virus in response to forskolin treatment as long as 7 weeks post-ACV withdrawal. (vi) Expression of HSV-1 productive genes (i.e. alpha0, **alpha4**, alpha27, UL30 and UL18) dropped precipitously in the presence of ACV and remained undetectable or continued to decline following its removal, whereas the levels of LAT and the host gene G3PDH remained relatively constant throughout the 31 day study period as measured by RT-PCR. These results indicate that QIF-PC12 cells offer a novel, neuronal cell culture system that may enhance our ability to study HSV-1 reactivation from a cryptic, latent-like, non-productive state in the absence of replication inhibitors.

8/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12091771 BIOSIS NO.: 199900386620
Conversion of US3-encoded protein kinase gene from pseudorabies virus in a diploid gene located within inverted repeats by genetic recombination between the viral genome isomers.
AUTHOR: Fernandez A; Menendez del Campo A M; Fernandez S; Camacho A; Castro J M; Tabares E(a)
AUTHOR ADDRESS: (a)Microbiologia, Facultad de Medicina, Universidad Autonoma de Madrid, Arzobispo Morcillo 4, 28029**Spain
JOURNAL: Virus Research 61 (2):p125-135 June, 1999
ISSN: 0168-1702
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The pseudorabies virus (PRV) genome consists of two components, long (UL) and short (US) regions. The US region is the only one capable of inverting itself relative to the UL region during productive infection, generating two equimolecular isomeric forms of viral DNA. Here we describe a recombinant virus (gIp2) generated by genetic recombination between pseudorabies viral isomers. This recombination event was observed in the parental virus gIS8, which was obtained by insertion of the **alpha4**-TK **herpes** simplex virus type 1 (HSV1) gene. The growth of gIS8 virus in the presence of 5-bromodeoxyuridine (BrdU) yielded gIp2. This was generated by nonhomologous recombination either between the two viral genomic isomers of gIS8, P and IUS, or between the same P isomer using nonhomologous and homologous recombination, with loss of the HSV1 sequences and duplication of the PRV US3-encoded protein kinase gene. Virus gIp2 is negative for TK, gI, gE, 11K and 28K and shows an in vitro replication capacity in neuronal cells approximately 22 times lower than that of parental virus gIS8, and similar to that of the Bartha vaccine virus strain in monkey kidney and human neuronal cells.

8/7/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11448525 BIOSIS NO.: 199800229857
Herpes simplex virus 1 induces and blocks apoptosis at multiple steps during infection and protects cells from exogenous inducers in a cell-type-dependent manner.
AUTHOR: Galvan Veronica; Roizman Bernard(a)
AUTHOR ADDRESS: (a)Marjorie B. Kovler Viral Oncol. Lab., Univ. Chicago, 910 E. 58th St., Chicago, IL 60637**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United

States of America 95 (7):p3931-3936 March 31, 1998
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Several publications have attested to the ability of **herpes** simplex viruses to protect cells against apoptosis. We investigated the ability of the virus to protect cells in continuous cultivation from apoptosis induced by the virus itself, and by other known inducers such as exposure to the tumor necrosis factor alpha (TNFalpha), antibody to Fas, C2-ceramide, osmotic shock (sorbitol), and thermal shock. The salient features of the results were that the virus was able to protect cells against apoptosis by all of the agents tested, and that apoptosis induced by the virus was a very early event that did not require de novo expression of viral genes. However, these events were cell-type specific. Thus: (i) The cell lines tested exhibited fragmented chromosomal DNA following infection with a virus lacking functional **alpha4** and US3 genes encoding the major regulatory protein and a viral protein kinase, respectively, but not by wild-type virus. (ii) Wild-type virus protected subcontinent SK-N-SH but not HeLa cells against induction of apoptosis by anti-Fas antibody, TNFalpha, C2-ceramide, and thermal shock. Confluent SK-N-SH cells were not protected from osmotic shock-induced apoptosis by wild-type infection. (iii) Wild-type virus protected SK-N-SH but not HeLa cells against induction of apoptosis by sorbitol, anti-Fas antibody, or TNFalpha and C2-ceramide. (iv) Mutant HSV-1(HFEM)tsB7 at the nonpermissive temperature infects cells but the DNA is not released from capsids, and therefore viral gene expression is restricted to the function of viral proteins introduced into the cell along with the capsid containing the viral DNA. HSV-1(HFEM)tsB7 induced apoptosis in Vero cells but not in SK-N-SH cells infected and maintained at 39.5degree C. (v) Tests of two caspase inhibitors showed that they blocked apoptosis induced by C2-ceramide and sorbitol, but were not able to block apoptosis induced by the virus lacking functional **alpha4** and US3 genes. We conclude that HSV-1 triggers apoptosis at multiple metabolic checkpoints and in turn has evolved mechanisms to block apoptosis at each point and that some of the pathways of induction are shared with exogenous inducers tested in this study whereas others are not.

8/7/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10758578 BIOSIS NO.: 199799379723
Therapy with antibody against leukocyte integrin **VLA-4** (CD49d) is effective and safe in virus-facilitated experimental allergic encephalomyelitis.
AUTHOR: Soilu-Hanninen M(a); Roytta M; Salmi A; Salonen R
AUTHOR ADDRESS: (a)Dep. Virology, Univ. Turku, Kiinamyllynkatu 13, FIN-20520 Turku**Finland
JOURNAL: Journal of Neuroimmunology 72 (1):p95-105 1997
ISSN: 0165-5728
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Experimental allergic encephalomyelitis (EAE) is facilitated in resistant BALB/c mice by intraperitoneal infection with an avirulent Semliki Forest virus (SFV-A7). Viral infection increases the incidence of EAE from 15-30% to 60-90% and speeds up appearance of paralysis from 24 to 14 days. In this paper, we describe treatment of virus-facilitated EAE with monoclonal antibodies (mAbs) against leukocyte and/or endothelial cell adhesion molecules. Therapy with mAb against ICAM-1 (intercellular adhesion molecule-1) had a modest effect, but caused hemorrhagic brain

and spinal cord lesions. Therapy with mAb against Mac-1 (alpha-M beta-2-integrin) was well tolerated but had no effect. Therapy with mAb against **VLA-4** (alpha-4-beta-1-integrin) was safe, diminished both clinical and histopathological signs of EAE, decreased induction of VCAM-1 (vascular cell adhesion molecule-1) on brain vessels and diminished infiltration of **VLA-4**+ cells into the brain. The amount of viral antigen in the brain was riot altered. We conclude that facilitation of leukocyte entry into the brain is a major mechanism for viral facilitation of EAE in the BALB/c mouse, and that facilitation can be inhibited by anti-adhesion therapy. This may have implications for treatment of relapses triggered by viral infections in multiple sclerosis.

8/7/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10451484 BIOSIS NO.: 199699072629
Therapy with antibody against leukocyte integrin **VLA-4** is effective and safe in virus facilitated EAE.
AUTHOR: Soilu-Hanninen Merja; Roytta Matias; Salmi Aimo; Salonen Reijo
AUTHOR ADDRESS: Dep. Virol., Univ. Turku, Kiinamyllynkatu 13, 20520 Turku **Finland
JOURNAL: Scandinavian Journal of Immunology 43 (6):p727 1996
CONFERENCE/MEETING: XXVIIth Meeting of the Scandinavian Society for Immunology Turku, Finland May 24-27, 1996
ISSN: 0300-9475
RECORD TYPE: Citation
LANGUAGE: English
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S7	95	(VLA(W)4 OR ALPHA4) AND(HERPES OR ARBOVIRUS)
S8	69	RD S7 (unique items)
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E12        2  AU=RUBIN SUSAN

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            4211  VLA(W)4
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 4/3/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.

10179605   BIOSIS NO.: 199698634523
Developmental injury to the cerebellum following perinatal Borna disease
  virus infection.
AUTHOR: Bautista Jan R; Rubin Steven A; Moran Timothy H; Schwartz
  Gary J; Carbone Kathryn M(a
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